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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,415	09/12/2003	Andrew Vaillant	16051-8US	6654

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EXAMINER	
HURT, SHARON L	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,415	VAILLANT ET AL.	
	Examiner	Art Unit	
	Sharon Hurt	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17,18,21,23 and 27-42* is/are pending in the application.

4a) Of the above claim(s) *3-13,33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,14,15,17,18,21,23,27-32,38,39,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *July 18, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Terminal Disclaimer

The terminal disclaimer filed on February 9, 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Amendment

The amendments filed May 24, 2007 has been entered. Claims 1, 14-15, 17-18, 21, 23 27-32 and 38 are currently amended. New claims 38-42 have been added.

Status of the Claims

Claims 1-15, 17-18, 21, 23, 27-38 and new claims 39-42 are pending. Claims 3-13 and 33-37 have been withdrawn. Claims 16, 19-20, 22 and 24-26 have been canceled. Claim 40 contains numerous distinct inventions therefore is withdrawn from consideration. Each sequence would require a different search in the art, which is a burden to the examiner. Claims 1-2, 14-15, 17-18, 21, 23, 27-32, 38 and new claims 39 and 41-42 are under examination.

Response to Arguments

The rejection of claims 1-2, 14-32 and 38 under 35 U.S.C. 103(a) as being unpatentable over Peyman et al. **is withdrawn**. Applicant's arguments filed May 24, 2007 have been fully considered and they are persuasive.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 14-15, 17-18, 21, 23, 27-32, 38-39 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement requirement**. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification does not enable the prophylaxis or treatment of a RSV or parainfluenza virus infection in a subject comprising administering to a subject in need of such treatment a therapeutically effective amount of **at least one** pharmacological acceptable oligonucleotide at least 10 nucleotides in length, ... The specification does not disclose treatment of a virus infection with **one** oligonucleotide.

The first paragraph of 35 U.S.C. 112 states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). The factors to be considered in determining whether undue experimentation is

required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those In the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a method of prophylaxis or treatment of RSV or parainfluenza virus infection in a subject by administering random sequence oligonucleotides that have antiviral activity.

The state of the prior art: The art teaches that oligonucleotide sequences, 10-40 nucleotides in length, may have antiviral activity. The art teaches that the oligonucleotides can be used to treat viral diseases. The art further teaches that randomers, 10 to 40 nucleotides in length, showed antiviral activity as described by Peyman et al. The art also teaches that a population of randomers can exhibit antiviral activity; however, it does not illustrate a single oligonucleotide effective as an antiviral agent.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings in the art regarding the structural and functional differences in the oligonucleotides, detailed teachings are required in the disclosure to enable the full scope of the claims. These teachings are absent. Applicant's disclosure is limited oligonucleotide randomers greater than 10 nucleotides in length. Examples are provided for randomers approximately 25 nucleotides in length; however, no examples are provided for one oligonucleotide.

The breadth of the claims and the quantity of experimentation needed: Because the invention encompasses at least oligonucleotide and because the specification fails to provide guidance as to how to use the claimed method for a single oligonucleotide other than oligonucleotides at least 10 nucleotides in length, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention commensurate in scope with the claims.

Claims 1-2, 14-15, 17-18, 21, 23, 27-32, 38-39 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **written description** rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e. **at least one pharmacological oligonucleotide at least 10 nucleotides in length.**

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* **a randomer, a few copies of any particular sequence in a preparation, at least 10 nucleotides in length**. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus.

However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species. In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is **at least one pharmacological oligonucleotide at least 10 nucleotides in length**. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (see *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

The specification does not provide a written description of a single oligonucleotide nor does it provide any blazemarks to guide those skilled in the art to select such a fragment out of the claimed invention. In *Forssmann v. Matsuo*, 23 USPQ2d 1548 (June 1, 1992), the description requirement became an issue with regard to the relation between a protein and a fragment thereof. The court indicated that although it provides adequate teachings to enable those skilled in art to make and use fragments, fails to contain written description for fragment of claim of patent in suit which complies with 35 USC 112, first paragraph, in that it provides neither motivation nor guidance to enable those skilled in the art to select fragment of the claim.

The skilled artisan cannot envision the detailed structure of a genus of compounds that are contemplated in the invention. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the

invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 14-15, 17-18, 21, 23, 27-32, 38 and new claim 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peyman et al. (US Patent 6,013,639) in view of Milligan et al. (Journal of Medicinal Chemistry, July 1993, Vol. 36, No. 14, pages 1923-1937).

The claimed invention is drawn to a method for the prophylaxis or treatment of a RSV or parainfluenza virus infection in a subject, preferably a human, comprising administering at least one pharmacologically acceptable oligonucleotide at least 10 nucleotides in length, wherein said oligonucleotide comprises at least one phosphorothioate linkage and wherein the anti-viral activity of said oligonucleotide occurs principally by a non-sequence mode of action, wherein the method comprises at least one antiviral randomer oligonucleotide, wherein said oligonucleotide is non complementary to any portion of the genomic sequence of RSV or parainfluenza virus, wherein said oligonucleotide is at least 40 nucleotides in length, wherein said oligonucleotide comprises at least one modification to the its chemical structure or at least one 2'-modification to the ribose moiety, wherein said oligonucleotide is double stranded, binds to one or more viral

components, wherein at least a portion of the sequence of said oligonucleotide is derived from a viral genome, wherein the method comprises a mixture of at least two different antiviral oligonucleotides.

Peyman et al. (hereinafter Peyman) discloses oligonucleotides where a nucleotide sequence is from 10 to 40 nucleotides in length and can be synthesized chemically. The oligonucleotides are used to treat diseases caused by viruses (Abstract). Stability can be effected by modifying or replacing the phosphate bridge (linkage). The most frequently used are phosphorothioate or methyl phosphonate bridges (Column 1, lines 25-35). Complete or partial replacement of the deoxyribose units, preferably, one, two, or three ribose units should be replaced ((column 4, lines 11-32). The oligonucleotides can be linked to molecules which are known to have a favorable influence on the properties of antisense oligonucleotides (column 4, lines 61-65). Oligonucleotides with chemical modifications demonstrate a higher cell uptake and increased stability (column 1, lines 38-50). The disclosed invention relates to the use of oligonucleotides possessing at least one terminal and modified pyrimidine nucleoside as diagnostic agents for detecting the presence or absence, or the quality, of a specific double-stranded or single-stranded nucleic acid molecule in a biological sample (column 6, lines 15-20).

Peyman teaches sense nucleotides, as well as antisense. While the antisense would be complementary, no part of the sense would be complementary to any part of the viral genome. Peyman does not teach that sense oligonucleotides have antiviral activity against viruses.

Milligan et al. (hereinafter Milligan) teaches about sense oligonucleotides and antisense oligonucleotides and their ability as potential antiviral applications (page 1923, Introduction). Milligan also teaches that in a study with control oligonucleotides, sense had a greater

antiproliferative effect than the antisense, indicating that a non-antisense mechanism may be responsible for the antiproliferative effect (page 1929, 1st column, 2nd full paragraph).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the sense oligonucleotides as taught by Milligan to treat RSV or parainfluenza with the composition taught by Peyman because it has been shown to be effective against viral infections. The person of ordinary skill in the art would have been motivated to use the pharmaceutical composition because Peyman and Milligan have demonstrated that it is effective against diseases caused by viruses, and reasonably would have expected success because of the teachings of Peyman and Milligan.

Response to Arguments

Applicants argue "nowhere is it taught or even suggested in Peyman that oligonucleotides have antiviral activity against multiple viruses acting by a non-sequence complementary mode of action". Peyman teaches oligonucleotides at least 10 nucleotides in length have antiviral activity. Milligan teaches that sense oligonucleotides or non-antisense oligonucleotides have antiproliferative effect. Applicants also argue "the sequences disclosed by Peyman, all of the sequences disclosed therein are antisenses". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., sequences) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

August 15, 2007

MARY E. MOSHER, PH.D.
PRIMARY EXAMINER